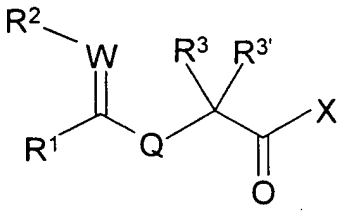
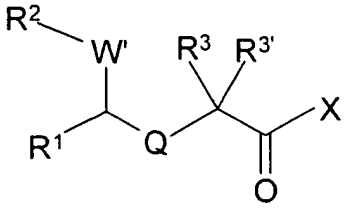
WHAT IS CLAIMED IS:

1. A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of formula Ia and/or Ib:



and



Ia Ib

wherein, in formula Ia, R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form an aryl, cycloalkenyl, heteroaryl or heterocyclic group having at least five atoms in the aryl, cycloalkenyl, heteroaryl or heterocyclic group and optionally containing or additionally containing in the case of heteroaryl and heterocyclic groups 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur, and wherein the heteroaryl or heterocyclic group is mono-cyclic;

in formula Ib, R^1 and R^2, together with the carbon atom and W' to which they are bound respectively, are joined to form a cycloalkyl, cycloalkenyl or heterocyclic group having at least five atoms in the cycloalkyl, cycloalkenyl or heterocyclic group and optionally containing or additionally containing in the case of the heterocyclic group 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur, and wherein the heterocyclic group is mono-cyclic;

and further wherein said aryl, cycloalkyl, cycloalkenyl, heteroaryl or heterocyclic group of formula Ia or Ib is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, $-OS(O)_2$-alkyl, $-OS(O)_2$-substituted alkyl, $-OS(O)_2$-aryl, $-OS(O)_2$-substituted aryl, $-OS(O)_2$-heteroaryl, $-OS(O)_2$-substituted heteroaryl, $-OS(O)_2$-heterocyclic, $-OS(O)_2$-substituted heterocyclic, $-OSO_2$-NRR where each R is independently hydrogen or alkyl, $-NRS(O)_2$-alkyl, $-NRS(O)_2$-substituted alkyl, $-NRS(O)_2$-aryl, $-NRS(O)_2$-substituted aryl, $-NRS(O)_2$-heteroaryl, $-NRS(O)_2$-substituted heteroaryl, $-NRS(O)_2$-heterocyclic, $-NRS(O)_2$-substituted heterocyclic, $-NRS(O)_2$-NR-alkyl, $-NRS(O)_2$-NR-substituted alkyl, $-NRS(O)_2$-NR-aryl, $-NRS(O)_2$-NR-substituted aryl, $-NRS(O)_2$-NR-heteroaryl, $-NRS(O)_2$-NR-substituted heteroaryl, $-NRS(O)_2$-NR-heterocyclic, $-NRS(O)_2$-NR-substituted heterocyclic where R is hydrogen or alkyl, $-N[S(O)_2-R']_2$ and $-N[S(O)_2-NR']_2$ where each R′ is independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^3 and $R^{3'}$ are independently selected from the group consisting of hydrogen, isopropyl, $-CH_2Z$ where Z is selected from the group consisting of hydrogen, hydroxyl, acylamino, alkyl, alkoxy, aryloxy, aryl, aryloxyaryl, carboxyl, carboxylalkyl, carboxyl-substituted alkyl, carboxyl-cycloalkyl, carboxyl-substituted cycloalkyl, carboxylaryl, carboxyl-substituted aryl, carboxylheteroaryl, carboxyl-substituted heteroaryl, carboxylheterocyclic, carboxyl-substituted heterocyclic, cycloalkyl, substituted alkyl, substituted alkoxy, substituted aryl, substituted aryloxy, substituted aryloxyaryl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic, and

where R^3 and $R^{3'}$ are joined to form a substituent selected from the group consisting of $=CHZ$ where Z is defined above provided that Z is not hydroxyl or thiol, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic and substituted heterocyclic;

Q is selected from the group consisting of -O-, -S-, -S(O)-, $-S(O)_2$, and $-NR^4$-;

R^4 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic or, optionally, R^4 and R^1 or R^4 and R^2, together with the atoms to which they are bound, are joined to form a heteroaryl, a substituted heteroaryl, a heterocyclic or a substituted heterocyclic group;

W is selected from the group consisting of nitrogen and carbon; and

W' is selected from the group consisting of nitrogen, carbon, oxygen, sulfur, S(O), and $S(O)_2$;

X is selected from the group consisting of hydroxyl, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, cycloalkoxy, substituted cycloalkoxy, cycloalkenoxy, substituted cycloalkenoxy, aryloxy, substituted aryloxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy,

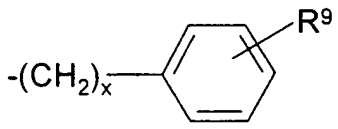
substituted heterocyclyloxy and -NR″R″ where each R″ is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof;

and further wherein the compound of formula Ia and/or Ib has a binding affinity to VLA-4 as expressed by an IC_{50} of about 15μM or less.

2. The method of Claim 1, wherein R^3 is -$(CH_2)_x$-Ar-R^9, where Ar is aryl, substituted aryl, heteroaryl and substituted heteroaryl; R^9 is selected from the group consisting acyl, acylamino, acyloxy, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, oxycarbonylamino, oxythiocarbonylamino, thioamidino, thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl, oxysulfonylamino and oxysulfonyl; and x is an integer from 0 to 4; and $R^{3'}$ is hydrogen.

3. The method of Claim 2, wherein R^3 is a group of the formula:



wherein R^9 and x are as defined in Claim 2.

4. The method of Claim 3, wherein R^9 is in the *para* position of the phenyl ring and x is an integer from 1 to 4.

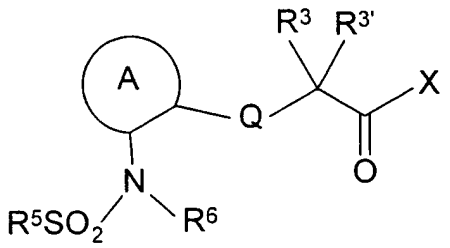
5. The method of Claim 4, wherein R^9 is selected from the group consisting of -O-Z-$NR^{11}R^{11'}$ and -O-Z-R^{12} wherein R^{11} and $R^{11'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R^{11} and $R^{11'}$ are joined to form a heterocycle or a substituted heterocycle, R^{12} is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of -C(O)- and -SO_2-.

6. The method of Claim 5, wherein Z is -C(O)-.

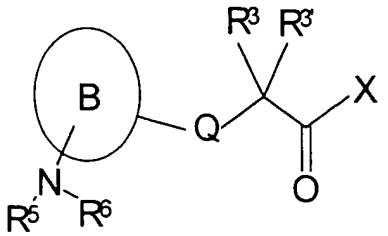
7. The method of Claim 6, wherein R^9 is -OC(O)$NR^{11}R^{11'}$.

8. The method of Claim 1, wherein Q is -NR^4-.

9. The method of Claim 1, wherein the compound has formula IIa or IIb:



IIa



IIb

wherein

ring A and ring B independently form a heteroaryl or substituted heteroaryl group having two nitrogen atoms in the heteroaryl ring;

R^5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and $-SO_2R^{10}$ where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

or optionally, one of, R^4 and ring A, R^4 and R^5, R^4 and R^6, or R^5 and R^6, together with the atoms to which they are bound, can be joined to form a heterocyclic or substituted heterocyclic ring;

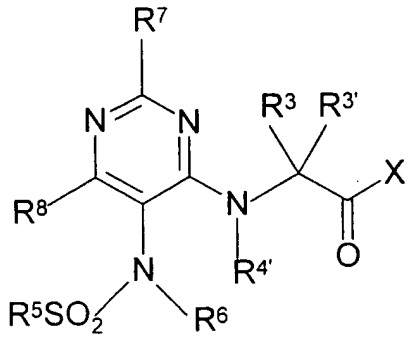
and enantiomers, diastereomers and pharmaceutically acceptable salts thereof; and provided that ring B does not form a 6-amino or substituted amino pyrimidin-4-yl group.

10. The method of Claim 9, wherein ring A forms a pyridazine, pyrimidine or pyrazine ring, wherein the pyridazine, pyrimidine or pyrazine ring is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen, and

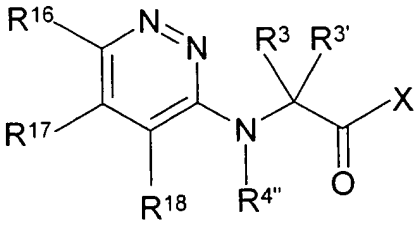
ring B forms a pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or a 1,1-dioxo-1,2,5-thiadiazole ring, wherein the pyridazine,

pyrimidine or pyrazine ring is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

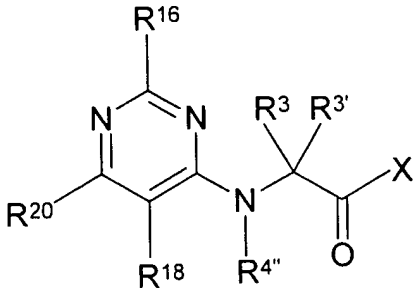
11. The method of Claim 1, wherein the compound has formula IIIa, IIIc, IIId, IIIe or IIIf:



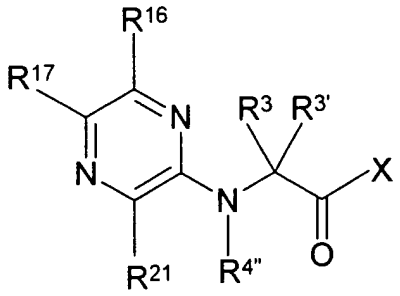
IIIa



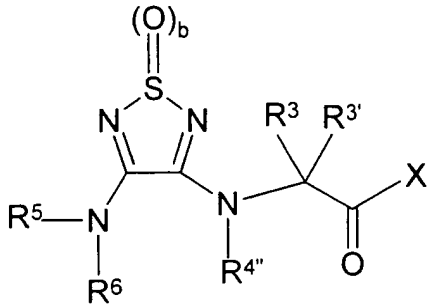
IIIc



IIId



IIIe



IIIf

wherein

$R^{4'}$ is selected from the group consisting of hydrogen and alkyl or, optionally, one of, $R^{4'}$ and R^5, $R^{4'}$ and R^6, R^5 and R^6, R^5 and R^8, or R^6 and R^8, together with the atoms to which they are bound, are joined to form a heterocyclic, a substituted heterocyclic, a heteroaryl or substituted heteroaryl group optionally containing from 1 to 3 additional hetero ring atoms selected from the group consisting of oxygen, nitrogen and sulfur;

$R^{4''}$ is selected from the group consisting of hydrogen and alkyl;

R^5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and $-SO_2R^{10}$ where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

R^7 and R^8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{16} and R^{17} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R^{18} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{20} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

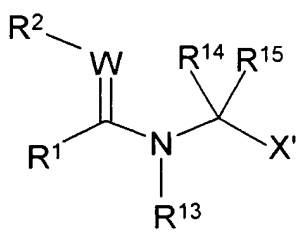
R^{21} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2;

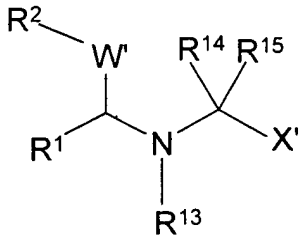
and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

12. The method of Claim 11, wherein the compound is selected from formula IIId, IIIe or IIIf.

13. A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of formula IVa and/or IVb:



and



IVa IVb

wherein, in formula IVa, R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form an aryl, cycloalkenyl, heteroaryl or heterocyclic group having at least five atoms in the aryl, cycloalkenyl, heteroaryl or heterocyclic group and optionally containing or additionally containing in the case of heteroaryl and heterocyclic groups 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur, and wherein the heteroaryl or heterocyclic group is mono-cyclic;

in formula IVb, R^1 and R^2, together with the carbon atom and W' to which they are bound respectively, are joined to form a cycloalkyl, cycloalkenyl or heterocyclic group having at least five atoms in the cycloalkyl, cycloalkenyl or heterocyclic group and optionally containing or additionally containing in the case the heterocyclic group 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur, and wherein the heterocyclic group is mono-cyclic;

and further wherein said aryl, cycloalkyl, cycloalkenyl, heteroaryl or heterocyclic group of formula IVa or IVb is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, $-OS(O)_2$-alkyl, $-OS(O)_2$-substituted alkyl, $-OS(O)_2$-aryl, $-OS(O)_2$-substituted aryl, $-OS(O)_2$-heteroaryl, $-OS(O)_2$-substituted heteroaryl, $-OS(O)_2$-heterocyclic, $-OS(O)_2$-substituted heterocyclic, $-OSO_2$-NRR where each R is independently hydrogen or alkyl, $-NRS(O)_2$-alkyl, $-NRS(O)_2$-substituted alkyl, $-NRS(O)_2$-aryl, $-NRS(O)_2$-substituted aryl, $-NRS(O)_2$-heteroaryl, $-NRS(O)_2$-substituted heteroaryl, $-NRS(O)_2$-heterocyclic, $-NRS(O)_2$-substituted heterocyclic, $-NRS(O)_2$-NR-alkyl, $-NRS(O)_2$-NR-substituted alkyl, $-NRS(O)_2$-NR-aryl, $-NRS(O)_2$-NR-substituted aryl, $-NRS(O)_2$-NR-heteroaryl, $-NRS(O)_2$-NR-substituted heteroaryl, $-NRS(O)_2$-NR-heterocyclic, $-NRS(O)_2$-NR-substituted heterocyclic where R is hydrogen or alkyl, $-N[S(O)_2-R']_2$ and $-N[S(O)_2-NR']_2$ where each R′ is independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{13} is selected from the group consisting of hydrogen, C_{1-10} alkyl, Cy, and Cy-C_{1-10} alkyl, wherein alkyl is optionally substituted with one to four substituents independently selected from R^a; and Cy is optionally substituted with one to four substituents independently selected from R^b;

R^{14} is selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, Cy, Cy-C_{1-10} alkyl, Cy-C_{2-10} alkenyl and Cy-C_{2-10} alkynyl, wherein alkyl, alkenyl, and alkynyl are optionally substituted with one to four substituents selected from phenyl and R^x, and Cy is optionally substituted with one to four substituents independently selected from R^y;

or R^{13}, R^{14} and the atoms to which they are attached together form a mono- or bicyclic ring containing 0-2 additional heteratoms selected from N, O and S;

R^{15} is selected from the group consisting of C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl, aryl-C_{1-10} alkyl, heteroaryl, heteroaryl-C_{1-10} alkyl, wherein alkyl, alkenyl and alkynyl are optionally substituted with one to four substituents selected from R^x, and aryl and heteroaryl are optionally substituted with one to four substituents independently selected from R^y;

or R^{14}, R^{15} and the carbon to which they are attached form a 3-7 membered mono- or bicyclic ring containing 0-2 heteroatoms selected from N, O and S;

R^a is selected from the group consisting of Cy and a group selected from R^x, wherein Cy is optionally substituted with one to four substituents independently selected from R^c;

R^b is selected from the group consisting of R^a, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl C_{1-10}alkyl, heteroaryl C_{1-10} alkyl, wherein alkyl, alkenyl, alkynyl, aryl, heteroaryl are optionally substituted with a group independently selected from R^c;

R^c is selected from the group consisting of halogen, NO_2, $C(O)OR^f$, C_{1-4} alkyl, C_{1-4} alkoxy, aryl, aryl C_{1-4} alkyl, aryloxy, heteroaryl, NR^fR^g, $R^fC(O)R^g$, $NR^fC(O)NR^fR^g$, and CN;

R^d and R^e are independently selected from hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, Cy and Cy C_{1-10}alkyl, wherein alkyl, alkenyl, alkynyl and Cy are optionally substituted with one to four substituents independently selected from R^c;

or R^d and R^e together with the atoms to which they are attached form a heterocyclic ring of 5 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and nitrogen;

R^f and R^g are independently selected from hydrogen, C_{1-10} alkyl, Cy and Cy-C_{1-10} alkyl wherein Cy is optionally substituted with C_{1-10} alkyl; or R^f and R^g together with the carbon to which they are attached form a ring of 5 to 7 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and nitrogen;

R^h is selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, cyano, aryl, aryl C_{1-10} alkyl, heteroaryl, heteroaryl C_{1-10} alkyl, and $-SO_2R^i$; wherein alkyl, alkenyl, and alkynl are optionally substituted with one to four substitutents independently selected from R^a; and aryl and heteroaryl are each optionally substituted with one to four substituents independently selected from R^b;

R^i is selected from the group consisting of C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, and aryl; wherein alkyl, alkenyl, alkynyl and aryl are each optionally substituted with one to four substituents independently selected from R^c;

R^x is selected from the group consisting of $-OR^d$, $-NO_2$, halogen, $-S(O)_mR^d$, $-SR^d$, $-S(O)_2OR^d$, $-S(O)_mNR^dR^e$, $-NR^dR^e$, $-O(CR^fR^g)_nNR^dR^e$, $-C(O)R^d$, $-CO_2R^d$; $-CO_2(CR^fR^g)_nCONR^dR^e$, $-OC(O)R^d$, -CN, $-C(O)NR^dR^e$, $-NR^dC(O)R^e$, $-OC(O)NR^dR^e$, $-NR^dC(O)OR^e$, $-NR^dC(O)NR^dR^e$, $-CR^d(N\text{-}OR^e)$, CF_3, oxo, $NR^dC(O)NR^dSO_2R^i$, $NR^dS(O)_mR^e$, $-OS(O)_2OR^d$, and $-OP(O)(OR^d)_2$;

R^y is selected from the group consisting of R^x, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl C_{1-10}alkyl, heteroaryl C_{1-10} alkyl, cycloalkyl,

heterocyclyl; wherein alkyl, alkenyl, alkynyl and aryl are each optionally substituted with one to four substitutents independently selected from R^x;

Cy is cycloalkyl, heterocyclyl, aryl, or heteroaryl;

m is an integer from 1 to 2;

n is an integer from 1 to 10;

W is selected from the group consisting of carbon and nitrogen;

W' is selected from the group consisting of carbon, nitrogen, oxygen, sulfur, S(O) and $S(O)_2$;

X' is selected from the group consisting of $-C(O)OR^d$, $-P(O)(OR^d)(OR^e)$, $-P(O)(R^d)(OR^e)$, $-S(O)_mOR^d$, $-C(O)NR^dR^h$, and -5-tetrazolyl;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof;

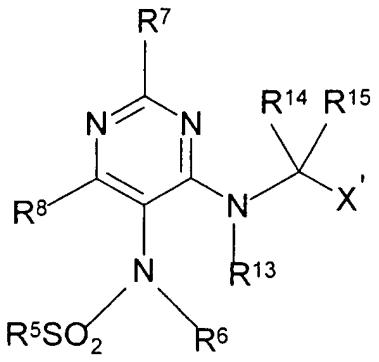
and further wherein the compound of formula IVa and/or IVb has a binding affinity to VLA-4 as expressed by an IC_{50} of about 15μM or less.

14. The method of Claim 13, wherein R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a heteroaryl or substituted heteroaryl group having two nitrogen atoms in the heteroaryl ring.

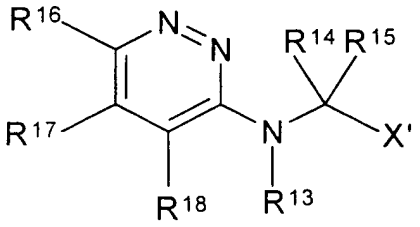
15. The method of Claim 14, wherein R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or 1,1-dioxo-1,2,5-thiadiazole ring; wherein the pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or 1,1-dioxo-1,2,5-thiadiazole ring is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

16. The method of Claim 13, wherein X' is $-C(O)OR^d$.

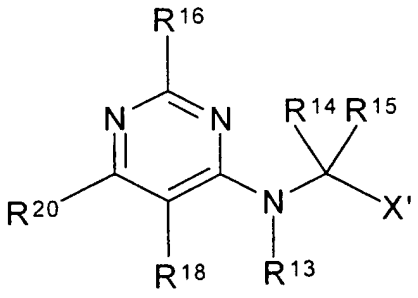
17. The method of Claim 13, wherein the compound has formula Va, Vc, Vd, Ve or Vf:



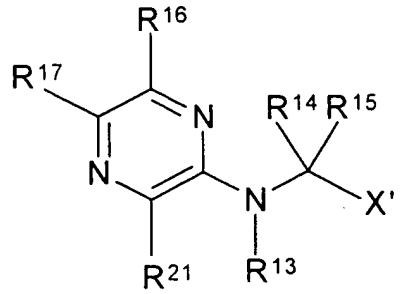
Va



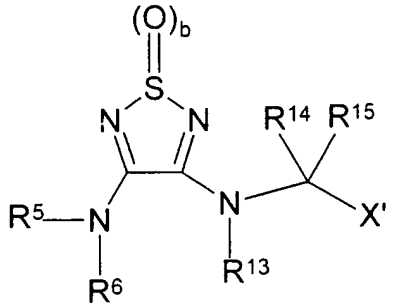
Vc



Vd



Ve



Vf

wherein

R^5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and $-SO_2R^{10}$ where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl; and

R^7 and R^8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl,

substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{16} and R^{17} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R^{18} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{20} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

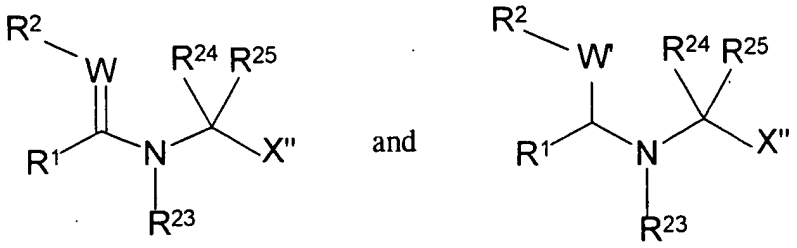
R^{21} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

18. The method of Claim 17, wherein the compound is selected from formula Vd, Ve or Vf.

19. A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of formula VIa and/or VIb:



VIa and VIb

wherein, in formula VIa, R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form an aryl, cycloalkenyl, heteroaryl or heterocyclic group having at least five atoms in the aryl, cycloalkenyl, heteroaryl or heterocyclic group and optionally containing or additionally containing in the case of heteroaryl and heterocyclic groups 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur, and wherein the heteroaryl or heterocyclic group is mono-cyclic;

in formula VIb, R^1 and R^2, together with the carbon atom and W' to which they are bound respectively, are joined to form a cycloalkyl, cycloalkenyl or heterocyclic group having at least five atoms in the cycloalkyl, cycloalkenyl or heterocyclic group and optionally containing or additionally containing in the case of the heterocyclic group 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur, and wherein the heterocyclic group is mono-cyclic;

and further wherein said aryl, cycloalkyl, cycloalkenyl, heteroaryl or heterocyclic group of formula VIa or VIb is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy,

substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, $-OS(O)_2$-alkyl, $-OS(O)_2$-substituted alkyl, $-OS(O)_2$-aryl, $-OS(O)_2$-substituted aryl, $-OS(O)_2$-heteroaryl, $-OS(O)_2$-substituted heteroaryl, $-OS(O)_2$-heterocyclic, $-OS(O)_2$-substituted heterocyclic, $-OSO_2$-NRR where each R is independently hydrogen or alkyl, $-NRS(O)_2$-alkyl, $-NRS(O)_2$-substituted alkyl, $-NRS(O)_2$-aryl, $-NRS(O)_2$-substituted aryl, $-NRS(O)_2$-heteroaryl, $-NRS(O)_2$-substituted heteroaryl, $-NRS(O)_2$-heterocyclic, $-NRS(O)_2$-substituted heterocyclic, $-NRS(O)_2$-NR-alkyl, $-NRS(O)_2$-NR-substituted alkyl, $-NRS(O)_2$-NR-aryl, $-NRS(O)_2$-NR-substituted aryl, $-NRS(O)_2$-NR-heteroaryl, $-NRS(O)_2$-NR-substituted heteroaryl, $-NRS(O)_2$-NR-heterocyclic, $-NRS(O)_2$-NR-substituted heterocyclic where R is hydrogen or alkyl, $-N[S(O)_2-R']_2$ and $-N[S(O)_2-NR']_2$ where each R′ is independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{23} is selected from the group consisting of hydrogen, C_{1-10} alkyl optionally substituted with one to four substituents independently selected from $R^{a'}$ and Cy optionally substituted with one to four substituents independently selected from $R^{b'}$;

R^{24} is selected from the group consisting of Ar^1-Ar^2-C_{1-10} alkyl, Ar^1-Ar^2-C_{2-10} alkenyl, Ar^1-Ar^2-C_{2-10} alkynyl, wherein Ar^1 and Ar^2 are independently aryl or heteroaryl each of which is optionally substituted with one to four substituents independently selected from $R^{b'}$; alkyl, alkenyl and

alkynyl are optionally substituted with one to four substituents independently selected from $R^{a'}$;

R^{25} is selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl, aryl C_{1-10}alkyl, heteroaryl, and heteroaryl C_{1-10} alkyl, wherein alkyl, alkenyl and alkynyl are optionally substituted with one to four substituents selected from $R^{a'}$, and aryl and heteroaryl are optionally substituted with one to four substituents independently selected from $R^{b'}$;

$R^{a'}$ is selected from the group consisting of Cy, $-OR^{d'}$, $-NO_2$, halogen $-S(O)_mR^{d'}$, $-SR^{d'}$, $-S(O)_2OR^{d'}$, $-S(O)_mNR^{d'}R^{e'}$, $-NR^{d'}R^{e'}$, $-O(CR^{f'}R^{g'})_nNR^{d'}R^{e'}$, $-C(O)R^{d'}$, $-CO_2R^{d'}$, $-CO_2(CR^{f'}R^{g'})_nCONR^{d'}R^{e'}$, $-OC(O)R^{d'}$, $-CN$, $-C(O)NR^{d'}R^{e'}$, $-NR^{d'}C(O)R^{e'}$, $-OC(O)NR^{d'}R^{e'}$, $-NR^{d'}C(O)OR^{e'}$, $-NR^{d'}C(O)NR^{d'}R^{e'}$, $-CR^{d'}(N\text{-}OR^{e'})$, CF_3, and $-OCF_3$;

wherein Cy is optionally substituted with one to four substituents independently selected from $R^{c'}$;

$R^{b'}$ is selected from the group consisting of $R^{a'}$, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl C_{1-10} alkyl, heteroaryl C_{1-10}alkyl,

wherein alkyl, alkenyl, aryl, heteroaryl are optionally substituted with a group independently selected from $R^{c'}$;

$R^{c'}$ is selected from the group consisting of halogen, amino, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, aryl, aryl C_{1-4}alkyl, hydroxy, CF_3, and aryloxy;

$R^{d'}$ and $R^{e'}$ are independently selected from hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, Cy and Cy C_{1-10}alkyl, wherein alkyl, alkenyl, alkynyl and Cy are optionally substituted with one to four substituents independently selected from $R^{c'}$; or $R^{d'}$ and $R^{e'}$ together with the atoms to which they are attached form a heterocyclic ring of 5 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and nitrogen;

$R^{f'}$ and $R^{g'}$ are independently selected from hydrogen, C_{1-10} alkyl, Cy and Cy-C_{1-10} alkyl; or $R^{f'}$ and $R^{g'}$ together with the carbon to which they are

attached form a ring of 5 to 7 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and nitrogen;

$R^{h'}$ is selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, cyano, aryl. aryl C_{1-10} alkyl, heteroaryl, heteroaryl C_{1-10} alkyl, or $-SO_2R^{i'}$;

wherein alkyl, alkenyl, and alkynyl are optionally substituted with one to four substitutents independently selected from $R^{a'}$; and aryl and heteroaryl are each optionally substituted with one to four substituents independently selected from $R^{b'}$;

$R^{i'}$ is selected from the group consisting of C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, and aryl;

wherein alkyl, alkenyl, alkynyl and aryl are each optionally substituted with one to four substituents independently selected from $R^{c'}$;

Cy is cycloalkyl, heterocyclyl, aryl, or heteroaryl;

X" is selected from the group consisting of $-C(O)OR^{d'}$, $-P(O)(OR^{d'})(OR^{e'})$, $-P(O)(R^{d'})(OR^{e'})$, $-S(O)_mOR^{d'}$, $-C(O)NR^{d'}R^{h'}$, and -5-tetrazolyl;

m is an integer from 1 to 2;

n is an integer from 1 to 10;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof;

and further wherein the compound of formula IVa and/or IVb has a binding affinity to VLA-4 as expressed by an IC_{50} of about 15μM or less.

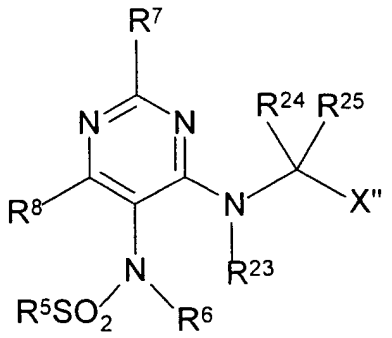
20. The method of Claim 19, wherein R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a heteroaryl or substituted heteroaryl group having two nitrogen atoms in the heteroaryl ring.

21. The method of Claim 20, wherein R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or 1,1-dioxo-1,2,5-thiadiazole ring; wherein the pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or 1,1-dioxo-1,2,5-thiadiazole ring is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

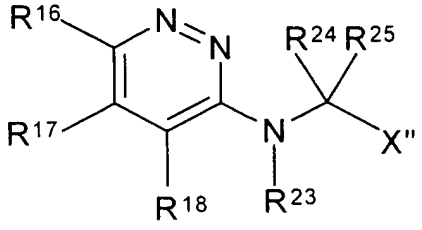
22. The method of Claim 19, wherein X" is $-C(O)OR^{d'}$.

23. The method of Claim 19, wherein R^{24} is $-CH_2-Ar^2-Ar^1$ and R^{25} is hydrogen.

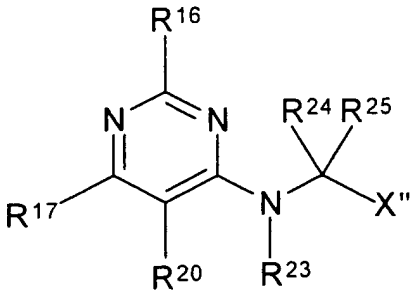
24. The method of Claim 19, wherein the compound has formula VIIa, VIIc, VIId, VIIe or VIIf:



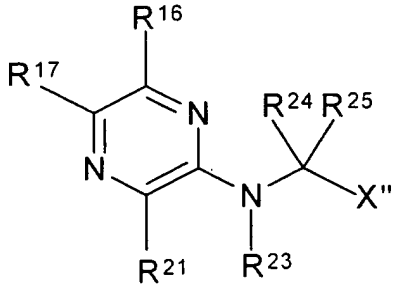
VIIa



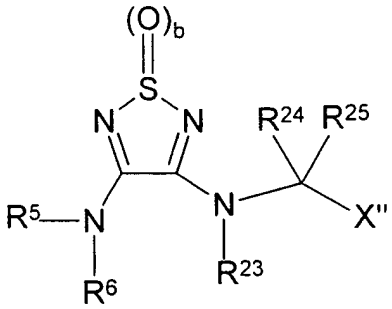
VIIc



VIId



VIIe



VIIf

wherein

R^5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl; aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl,

heteroaryl, substituted heteroaryl, and $-SO_2R^{10}$ where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl; and

R^7 and R^8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{16} and R^{17} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R^{18} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{20} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{21} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

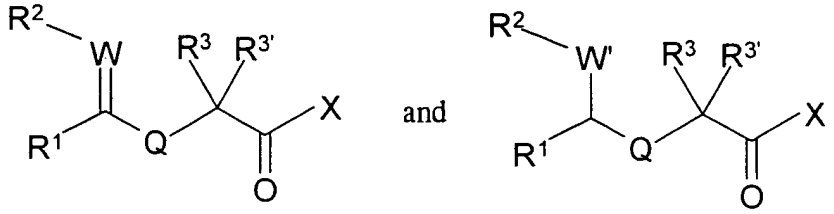
b is 1 or 2;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

25. The method of Claim 24, wherein the compound is selected from formula VIId, VIIe or VIIf.

26. The method of Claims 1, 13 or 19, wherein the disease mediated by VLA-4 is an inflammatory disease.

27. A compound of formula Ia and/or Ib:



Ia Ib

wherein, in formula Ia, R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form an aryl, cycloalkenyl, heteroaryl or heterocyclic group having at least five atoms in the aryl, cycloalkenyl, heteroaryl or heterocyclic group and optionally containing or additionally containing in the case of heteroaryl and heterocyclic groups 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur, and wherein the heteroaryl or heterocyclic group is mono-cyclic;

in formula Ib, R^1 and R^2, together with the carbon atom and W' to which they are bound respectively, are joined to form a cycloalkyl, cycloalkenyl or heterocyclic group having at least five atoms in the cycloalkyl, cycloalkenyl or heterocyclic group and optionally containing or additionally containing in the case of the heterocyclic group 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur, and wherein the heterocyclic group is mono-cyclic;

and further wherein said aryl, cycloalkyl, cycloalkenyl, heteroaryl or heterocyclic group of formula Ia or Ib is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group

consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, $-OS(O)_2$-alkyl, $-OS(O)_2$-substituted alkyl, $-OS(O)_2$-aryl, $-OS(O)_2$-substituted aryl, $-OS(O)_2$-heteroaryl, $-OS(O)_2$-substituted heteroaryl, $-OS(O)_2$-heterocyclic, $-OS(O)_2$-substituted heterocyclic, $-OSO_2$-NRR where each R is independently hydrogen or alkyl, $-NRS(O)_2$-alkyl, $-NRS(O)_2$-substituted alkyl, $-NRS(O)_2$-aryl, $-NRS(O)_2$-substituted aryl, $-NRS(O)_2$-heteroaryl, $-NRS(O)_2$-substituted heteroaryl, $-NRS(O)_2$-heterocyclic, $-NRS(O)_2$-substituted heterocyclic, $-NRS(O)_2$-NR-alkyl, $-NRS(O)_2$-NR-substituted alkyl, $-NRS(O)_2$-NR-aryl, $-NRS(O)_2$-NR-substituted aryl, $-NRS(O)_2$-NR-heteroaryl, $-NRS(O)_2$-NR-substituted heteroaryl, $-NRS(O)_2$-NR-heterocyclic, $-NRS(O)_2$-NR-substituted heterocyclic where R is hydrogen or alkyl, $-N[S(O)_2-R']_2$ and $-N[S(O)_2-NR']_2$ where each R′ is independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^3 is $-(CH_2)_x$-Ar-R^9, where Ar is aryl, substituted aryl, heteroaryl and substituted heteroaryl; R^9 is selected from the group consisting of acyl, acylamino, acyloxy, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, oxycarbonylamino,

oxythiocarbonylamino, thioamidino, thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl, oxysulfonylamino and oxysulfonyl; and x is an integer from 0 to 4;

$R^{3'}$ is selected from the group consisting of hydrogen, isopropyl, $-CH_2Z$ where Z is selected from the group consisting of hydrogen, hydroxyl, acylamino, alkyl, alkoxy, aryloxy, aryl, aryloxyaryl, carboxyl, carboxylalkyl, carboxyl-substituted alkyl, carboxyl-cycloalkyl, carboxyl-substituted cycloalkyl, carboxylaryl, carboxyl-substituted aryl, carboxylheteroaryl, carboxyl-substituted heteroaryl, carboxylheterocyclic, carboxyl-substituted heterocyclic, cycloalkyl, substituted alkyl, substituted alkoxy, substituted aryl, substituted aryloxy, substituted aryloxyaryl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

Q is selected from the group consisting of -O-, -S-, -S(O)-, $-S(O)_2$, and $-NR^4-$;

R^4 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic or, optionally, R^4 and R^1 or R^4 and R^2, together with the atoms to which they are bound, are joined to form a heteroaryl, a substituted heteroaryl, a heterocyclic or a substituted heterocyclic group;

W is selected from the group consisting of nitrogen and carbon; and

W' is selected from the group consisting of nitrogen, carbon, oxygen, sulfur, S(O), and $S(O)_2$;

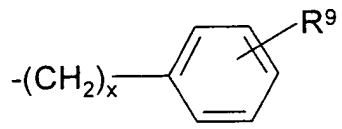
X is selected from the group consisting of hydroxyl, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, cycloalkoxy, substituted cycloalkoxy, cycloalkenoxy, substituted cycloalkenoxy, aryloxy, substituted aryloxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy and -NR"R" where each R" is independently

selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

and enantiomers, diasteromers and pharmaceutically acceptable salts thereof;

and further wherein the compound of formula Ia and/or Ib has a binding affinity to VLA-4 as expressed by an IC_{50} of about 15μM or less.

28. The compound of Claim 27, wherein R^3 is a group of the formula:



wherein R^9 and x are as defined in Claim 27; and $R^{3'}$ is hydrogen.

29. The compound of Claim 28, wherein R^9 is in the *para* position of the phenyl ring, and x is an integer from 1 to 4.

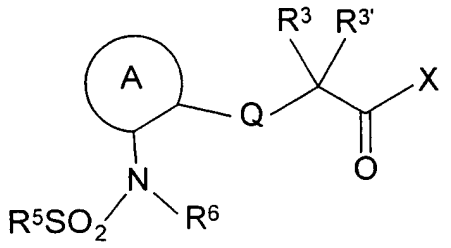
30. The compound of Claim 29, wherein R^9 is selected from the group consisting of -O-Z-$NR^{11}R^{11'}$ and -O-Z-R^{12} wherein R^{11} and $R^{11'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R^{11} and $R^{11'}$ are joined to form a heterocycle or a substituted heterocycle, R^{12} is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of -C(O)- and -SO_2-.

31. The compound of Claim 30, wherein Z is -C(O)-.

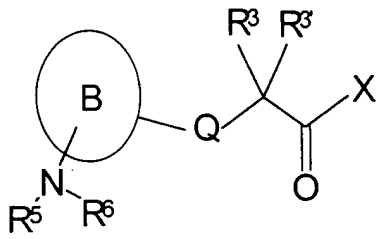
32. The compound of Claim 31, wherein R^9 is $-OC(O)NR^{11}R^{11'}$.

33. The compound of Claim 27, wherein Q is $-NR^4-$.

34. The compound of Claim 27, wherein the compound has formula IIa or IIb:



IIa



IIb

wherein

ring A and ring B independently form a heteroaryl or substituted heteroaryl group having two nitrogen atoms in the heteroaryl ring;

R^5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and $-SO_2R^{10}$ where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

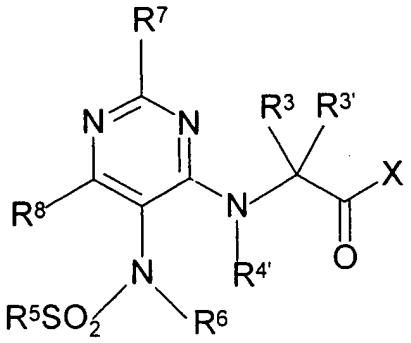
or optionally, one of, R^4 and ring A, R^4 and R^5, R^4 and R^6, or R^5 and R^6, together with the atoms to which they are bound, can be joined to form a heterocyclic or substituted heterocyclic ring;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof; and provided that ring B does not form a 6-amino or substituted amino pyrimidin-4-yl group.

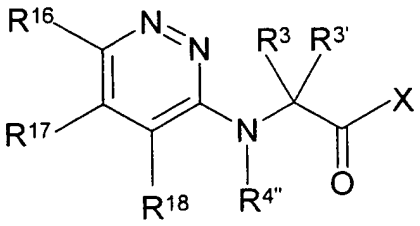
35. The compound of Claim 34, wherein ring A forms a pyridazine, pyrimidine or pyrazine ring, wherein the pyridazine, pyrimidine or pyrazine ring is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen, and

ring B forms a pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or a 1,1-dioxo-1,2,5-thiadiazole ring, wherein the pyridazine, pyrimidine or pyrazine ring is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

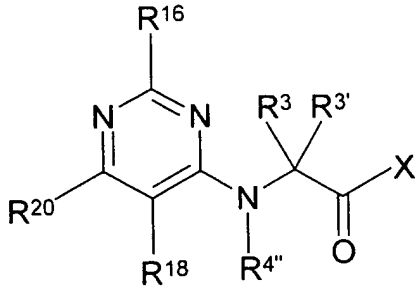
36. The compound of Claim 27, wherein the compound has formula IIIa, IIIc, IIId, IIIe or IIIf:



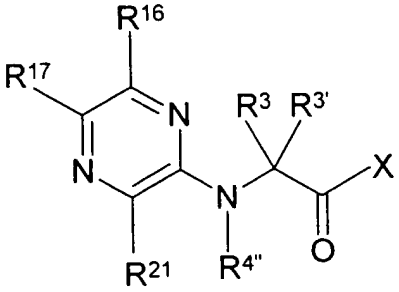
IIIa



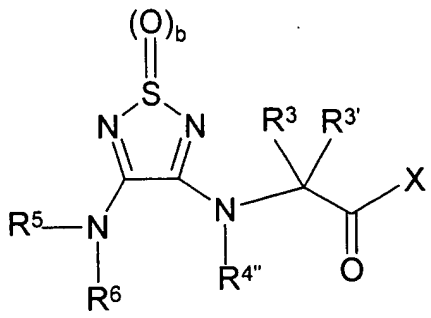
IIIc



IIId



IIIe



IIIf

wherein

$R^{4'}$ is selected from the group consisting of hydrogen and alkyl or, optionally, one of, $R^{4'}$ and R^5, $R^{4'}$ and R^6, R^5 and R^6, R^5 and R^8, or R^6 and R^8, together with the atoms to which they are bound, are joined to form a heterocyclic, a substituted heterocyclic, a heteroaryl or substituted heteroaryl group optionally containing from 1 to 3 additional hetero ring atoms selected from the group consisting of oxygen, nitrogen and sulfur;

$R^{4''}$ is selected from the group consisting of hydrogen and alkyl;

R^5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and $-SO_2R^{10}$ where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

R^7 and R^8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl,

substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{16} and R^{17} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R^{18} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{20} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

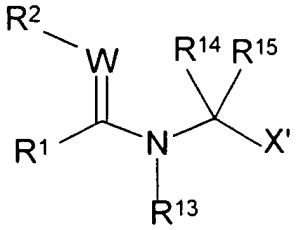
R^{21} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

37. The compound of Claim 36, wherein the compound is selected from formula IIId, IIIe or IIIf.

38. A compound of formula IVa:



IVa

wherein R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a heteroaryl group having two nitrogen atoms in the heteroaryl ring;

and further wherein said heteroaryl group is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, $-OS(O)_2$-alkyl, $-OS(O)_2$-substituted alkyl, $-OS(O)_2$-aryl, $-OS(O)_2$-substituted aryl, $-OS(O)_2$-heteroaryl, $-OS(O)_2$-substituted heteroaryl, $-OS(O)_2$-heterocyclic, $-OS(O)_2$-substituted heterocyclic, $-OSO_2$-NRR where each R is independently hydrogen or alkyl, $-NRS(O)_2$-alkyl, $-NRS(O)_2$-substituted alkyl, $-NRS(O)_2$-aryl, $-NRS(O)_2$-substituted aryl, $-NRS(O)_2$-heteroaryl, $-NRS(O)_2$-substituted heteroaryl, $-NRS(O)_2$-heterocyclic, $-NRS(O)_2$-substituted heterocyclic, $-NRS(O)_2$-NR-alkyl, $-NRS(O)_2$-NR-substituted alkyl, $-NRS(O)_2$-NR-aryl, $-NRS(O)_2$-NR-substituted aryl, $-NRS(O)_2$-NR-heteroaryl, $-NRS(O)_2$-NR-substituted heteroaryl, $-NRS(O)_2$-NR-heterocyclic, $-NRS(O)_2$-NR-substituted heterocyclic where R is hydrogen or alkyl, $-N[S(O)_2-R']_2$ and $-N[S(O)_2-NR']_2$ where each R′ is independently selected from the group consisting of alkyl, substituted alkyl,

aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{13} is selected from the group consisting of hydrogen, C_{1-10} alkyl, Cy, and Cy-C_{1-10} alkyl, wherein alkyl is optionally substituted with one to four substituents independently selected from R^a; and Cy is optionally substituted with one to four substituents independently selected from R^b;

R^{14} is selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, Cy, Cy-C_{1-10} alkyl, Cy-C_{2-10} alkenyl and Cy-C_{2-10} alkynyl, wherein alkyl, alkenyl, and alkynyl are optionally substituted with one to four substituents selected from phenyl and R^x, and Cy is optionally substituted with one to four substituents independently selected from R^y;

or R^{13}, R^{14} and the atoms to which they are attached together form a mono- or bicyclic ring containing 0-2 additional heteratoms selected from N, O and S;

R^{15} is selected from the group consisting of C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl, aryl-C_{1-10} alkyl, heteroaryl, heteroaryl-C_{1-10} alkyl, wherein alkyl, alkenyl and alkynyl are optionally substituted with one to four substituents selected from R^x, and aryl and heteroaryl are optionally substituted with one to four substituents independently selected from R^y;

or R^{14}, R^{15} and the carbon to which they are attached form a 3-7 membered mono- or bicyclic ring containing 0-2 heteroatoms selected from N, O and S;

R^a is selected from the group consisting of Cy and a group selected from R^x, wherein Cy is optionally substituted with one to four substituents independently selected from R^c;

R^b is selected from the group consisting of R^a, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl C_{1-10}alkyl, heteroaryl C_{1-10} alkyl, wherein alkyl, alkenyl, alkynyl, aryl, heteroaryl are optionally substituted with a group independently selected from R^c;

R^c is selected from the group consisting of halogen, NO_2, $C(O)OR^f$,

C_{1-4} alkyl, C_{1-4} alkoxy, aryl, aryl C_{1-4} alkyl, aryloxy, heteroaryl, NR^fR^g, $R^fC(O)R^g$, $NR^fC(O)NR^fR^g$, and CN;

R^d and R^e are independently selected from hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, Cy and Cy C_{1-10}alkyl, wherein alkyl, alkenyl, alkynyl and Cy are optionally substituted with one to four substituents independently selected from R^c;

or R^d and R^e together with the atoms to which they are attached form a heterocyclic ring of 5 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and nitrogen;

R^f and R^g are independently selected from hydrogen, C_{1-10} alkyl, Cy and Cy-C_{1-10} alkyl wherein Cy is optionally substituted with C_{1-10} alkyl; or R^f and R^g together with the carbon to which they are attached form a ring of 5 to 7 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and nitrogen;

R^h is selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, cyano, aryl, aryl C_{1-10} alkyl, heteroaryl, heteroaryl C_{1-10} alkyl, and $-SO_2R^i$; wherein alkyl, alkenyl, and alkynl are optionally substituted with one to four substitutents independently selected from R^a; and aryl and heteroaryl are each optionally substituted with one to four substituents independently selected from R^b;

R^i is selected from the group consisting of C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, and aryl; wherein alkyl, alkenyl, alkynyl and aryl are each optionally substituted with one to four substituents independently selected from R^c;

R^x is selected from the group consisting of $-OR^d$, $-NO_2$, halogen, $-S(O)_mR^d$, $-SR^d$, $-S(O)_2OR^d$, $-S(O)_mNR^dR^e$, $-NR^dR^e$, $-O(CR^fR^g)_nNR^dR^e$, $-C(O)R^d$, $-CO_2R^d$, $-CO_2(CR^fR^g)_nCONR^dR^e$, $-OC(O)R^d$, -CN, $-C(O)NR^dR^e$, $-NR^dC(O)R^e$, $-OC(O)NR^dR^e$, $-NR^dC(O)OR^e$, $-NR^dC(O)NR^dR^e$, $-CR^d(N\text{-}OR^e)$, CF_3, oxo, $NR^dC(O)NR^dSO_2R^i$, $NR^dS(O)_mR^e$, $-OS(O)_2OR^d$, and $-OP(O)(OR^d)_2$;

R^y is selected from the group consisting of R^x, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl C_{1-10}alkyl, heteroaryl C_{1-10} alkyl, cycloalkyl, heterocyclyl; wherein alkyl, alkenyl, alkynyl and aryl are each optionally substituted with one to four substitutents independently selected from R^x;

Cy is cycloalkyl, heterocyclyl, aryl, or heteroaryl;

m is an integer from 1 to 2;

n is an integer from 1 to 10;

W is selected from the group consisting of carbon and nitrogen;

W' is selected from the group consisting of carbon, nitrogen, oxygen, sulfur, S(O) and $S(O)_2$;

X' is selected from the group consisting of $-C(O)OR^d$, $-P(O)(OR^d)(OR^e)$, $-P(O)(R^d)(OR^e)$, $-S(O)_mOR^d$, $-C(O)NR^dR^h$, and -5-tetrazolyl;

and enatiomers, diastereomers and pharmaceutically acceptable salts thereof;

and further wherein the compound of formula IV has a binding affinity to VLA-4 as expressed by an IC_{50} of about 15μM or less;

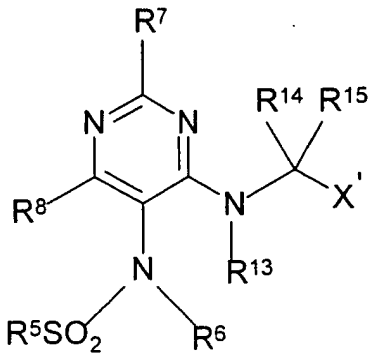
and provided that when R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a 2-arylpyrimidin-4-yl group and R^{14} is hydrogen, then R^{15} is not alkyl of from 1 to 6 carbon atoms optionally substituted with hydroxyl; and when R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a 5-arylpyrazin-2-yl group and R^{14} is hydrogen, then R^{15} is not 4-hydroxybenzyl.

39. The compound of Claim 38, wherein R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or 1,1-dioxo-1,2,5-thiadiazole ring; wherein the pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or a 1,1-dioxo-1,2,5-thiadiazole ring is optionally

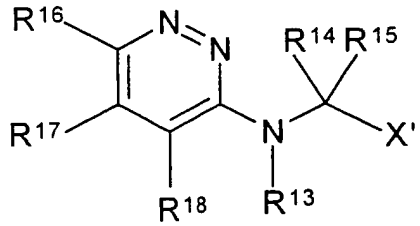
substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

40. The compound of Claim 38, wherein X' is $-C(O)OR^d$.

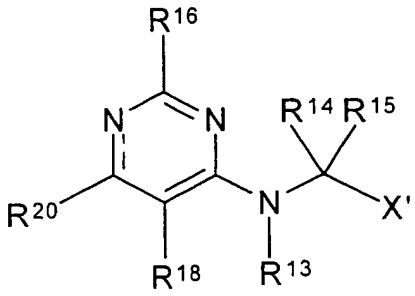
41. The compound of Claim 38, wherein the compound has formula Va, Vc, Vd, Ve or Vf:



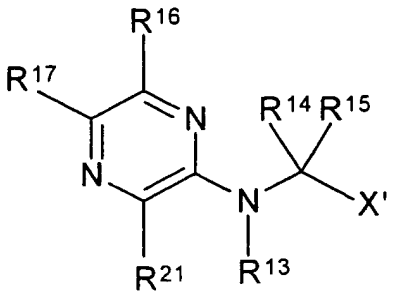
Va



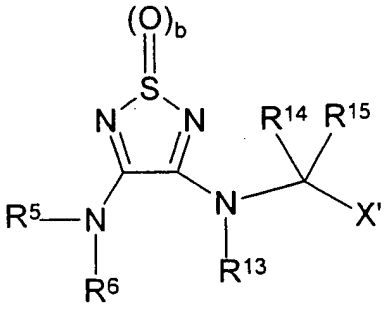
Vc



Vd



Ve



Vf

wherein

R^5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and $-SO_2R^{10}$ where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl; and

R^7 and R^8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{16} and R^{17} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R^{18} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{20} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

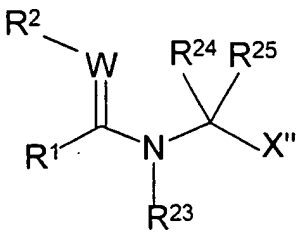
R^{21} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2;

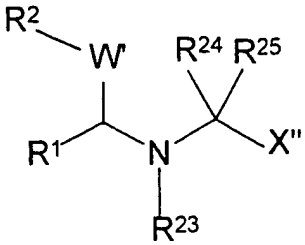
and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

42. The compound of Claim 41, wherein the compound is selected from formula Vd, Ve or Vf.

43. A compound of formula VIa and/or VIb:



and



VIa VIb

wherein, in formula VIa, R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form an aryl, cycloalkenyl, heteroaryl or heterocyclic group having at least five atoms in the aryl, cycloalkenyl, heteroaryl or heterocyclic group and optionally containing or additionally containing in the case of heteroaryl and heterocyclic groups 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur, and wherein the heteroaryl or heterocyclic group is mono-cyclic;

in formula VIb, R^1 and R^2, together with the carbon atom and W' to which they are bound respectively, are joined to form a cycloalkyl, cycloalkenyl or heterocyclic group having at least five atoms in the cycloalkyl, cycloalkenyl or heterocyclic group and optionally containing or additionally containing in the case of the heterocyclic group 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur, and wherein the heterocyclic group is mono-cyclic;

and further wherein said aryl, cycloalkyl, cycloalkenyl, heteroaryl or heterocyclic group of formula VIa or VIb is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino,

aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, $-OS(O)_2$-alkyl, $-OS(O)_2$-substituted alkyl, $-OS(O)_2$-aryl, $-OS(O)_2$-substituted aryl, $-OS(O)_2$-heteroaryl, $-OS(O)_2$-substituted heteroaryl, $-OS(O)_2$-heterocyclic, $-OS(O)_2$-substituted heterocyclic, $-OSO_2$-NRR where each R is independently hydrogen or alkyl, $-NRS(O)_2$-alkyl, $-NRS(O)_2$-substituted alkyl, $-NRS(O)_2$-aryl, $-NRS(O)_2$-substituted aryl, $-NRS(O)_2$-heteroaryl, $-NRS(O)_2$-substituted heteroaryl, $-NRS(O)_2$-heterocyclic, $-NRS(O)_2$-substituted heterocyclic, $-NRS(O)_2$-NR-alkyl, $-NRS(O)_2$-NR-substituted alkyl, $-NRS(O)_2$-NR-aryl, $-NRS(O)_2$-NR-substituted aryl, $-NRS(O)_2$-NR-heteroaryl, $-NRS(O)_2$-NR-substituted heteroaryl, $-NRS(O)_2$-NR-heterocyclic, $-NRS(O)_2$-NR-substituted heterocyclic where R is hydrogen or alkyl, $-N[S(O)_2-R']_2$ and $-N[S(O)_2-NR']_2$ where each R′ is independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{23} is selected from the group consisting of hydrogen, C_{1-10} alkyl optionally substituted with one to four substituents independently selected from $R^{a'}$ and Cy optionally substituted with one to four substituents independently selected from $R^{b'}$;

R^{24} is selected from the group consisting of Ar^1-Ar^2-C_{1-10} alkyl, Ar^1-Ar^2-C_{2-10} alkenyl, Ar^1-Ar^2-C_{2-10} alkynyl, wherein Ar^1 and Ar^2 are independently aryl or heteroaryl each of which is optionally substituted with

one to four substituents independently selected from $R^{b'}$; alkyl, alkenyl and alkynyl are optionally substituted with one to four substituents independently selected from $R^{a'}$;

R^{25} is selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl, aryl C_{1-10}alkyl, heteroaryl, and heteroaryl C_{1-10} alkyl, wherein alkyl, alkenyl and alkynyl are optionally substituted with one to four substituents selected from $R^{a'}$, and aryl and heteroaryl are optionally substituted with one to four substituents independently selected from $R^{b'}$;

$R^{a'}$ is selected from the group consisting of Cy, $-OR^{d'}$, $-NO_2$, halogen $-S(O)_mR^{d'}$, $-SR^{d'}$, $-S(O)_2OR^{d'}$, $-S(O)_mNR^{d'}R^{e'}$, $-NR^{d'}R^{e'}$, $-O(CR^{f'}R^{g'})_nNR^{d'}R^{e'}$, $-C(O)R^{d'}$, $-CO_2R^{d'}$, $-CO_2(CR^{f'}R^{g'})_nCONR^{d'}R^{e'}$, $-OC(O)R^{d'}$, -CN, $-C(O)NR^{d'}R^{e'}$, $-NR^{d'}C(O)R^{e'}$, $-OC(O)NR^{d'}R^{e'}$, $-NR^{d'}C(O)OR^{e'}$, $-Nr^{d'}C(O)NR^{d'}R^{e'}$, $-CR^{d'}(N-OR^{e'})$, CF_3, and $-OCF_3$;

wherein Cy is optionally substituted with one to four substituents independently selected from $R^{c'}$;

$R^{b'}$ is selected from the group consisting of $R^{a'}$, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl C_{1-10} alkyl, heteroaryl C_{1-10}alkyl,

wherein alkyl, alkenyl, aryl, heteroaryl are optionally substituted with a group independently selected from $R^{c'}$;

$R^{c'}$ is selected from the group consisting of halogen, amino, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, aryl, aryl C_{1-4}-alkyl, hydroxy, CF_3, and aryloxy;

$R^{d'}$ and $R^{e'}$ are independently selected from hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, Cy and Cy C_{1-10}alkyl, wherein alkyl, alkenyl, alkynyl and Cy are optionally substituted with one to four substituents independently selected from $R^{c'}$; or $R^{d'}$ and $R^{e'}$ together with the atoms to which they are attached form a heterocyclic ring of 5 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and nitrogen;

$R^{f'}$ and $R^{g'}$ are independently selected from hydrogen, C_{1-10} alkyl, Cy and Cy-C_{1-10} alkyl; or $R^{f'}$ and $R^{g'}$ together with the carbon to which they are

attached form a ring of 5 to 7 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and nitrogen;

$R^{h'}$ is selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, cyano, aryl, aryl C_{1-10} alkyl, heteroaryl, heteroaryl C_{1-10} alkyl, or $-SO_2R^{i'}$;

wherein alkyl, alkenyl, and alkynyl are optionally substituted with one to four substitutents independently selected from $R^{a'}$; and aryl and heteroaryl are each optionally substituted with one to four substituents independently selected from $R^{b'}$;

$R^{i'}$ is selected from the group consisting of C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, and aryl;

wherein alkyl, alkenyl, alkynyl and aryl are each optionally substituted with one to four substituents independently selected from $R^{c'}$;

Cy is cycloalkyl, heterocyclyl, aryl, or heteroaryl;

X" is selected from the group consisting of $-C(O)OR^{d'}$, $-P(O)(OR^{d'})(OR^{e'})$, $-P(O)(R^{d'})(OR^{e'})$, $-S(O)_mOR^{d'}$, $-C(O)NR^{d'}R^{h'}$, and -5-tetrazolyl;

m is an integer from 1 to 2;

n is an integer from 1 to 10;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof;

and further wherein the compounds of formula VIa and/or VIb have a binding affinity to VLA-4 as expressed by an IC_{50} of about 15μM or less.

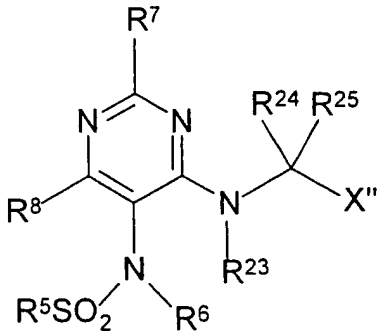
44. The compound of Claim 43, wherein R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a heteroaryl or substituted heteroaryl group having two nitrogen atoms in the heteroaryl ring.

45. The compound of Claim 44, wherein R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or 1,1-dioxo-1,2,5-thiadiazole ring; wherein the pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or 1,1-dioxo-1,2,5-thiadiazole ring is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

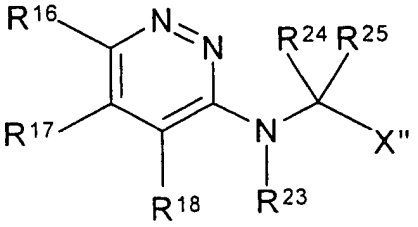
46. The compound of Claim 43, wherein X" is $-C(O)OR^{d'}$.

47. The compound of Claim 43, wherein R^{24} is $-CH_2-Ar^2-Ar^1$ and R^{25} is hydrogen.

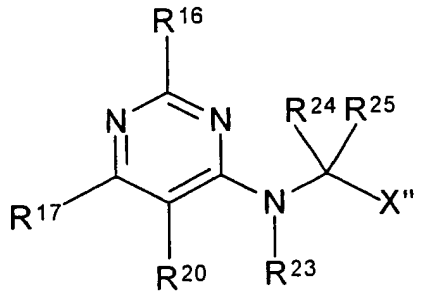
48. The compound of Claim 43, wherein the compound has formula VIIa, VIIc, VIId, VIIe or VIIf:



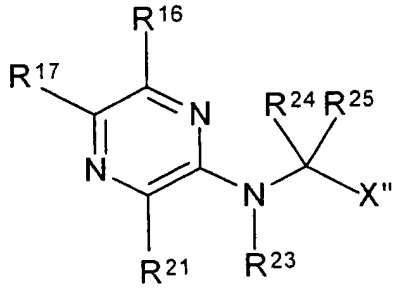
VIIa



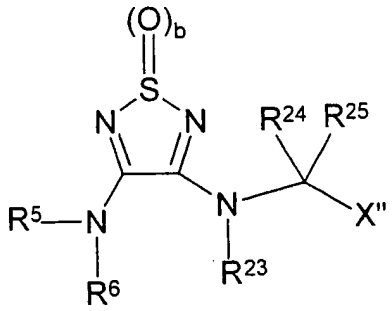
VIIc



VIId



VIIe



VIIf

wherein

R^5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl,

heteroaryl, substituted heteroaryl, and $-SO_2R^{10}$ where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl; and

R^7 and R^8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{16} and R^{17} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R^{18} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{20} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{21} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

49. The compound of Claim 48, wherein the compound is selected from formula VIId, VIIe or VIIf.

50. A compound selected from the group consisting of:

N-(2-chloro-5-nitropyrimidin-4-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-[5-(*N*-4-toluenesulfonylamino)pyrimidin-4-yl]-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine *tert*-butyl ester,

N-[5-(*N*-4-toluenesulfonylamino)pyrimidin-4-yl]-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-[5-(*N*-methyl-*N*-4-toluenesulfonylamino)pyrimidin-4-yl]-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine *tert*-butyl ester,

N-[5-(*N*-methyl-*N*-4-toluenesulfonylamino)pyrimidin-4-yl]-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-[5-(*N*,*N*-di-4-toluenesulfonylamino)pyrimidin-4-yl]-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-[5-[*N*-(1-*N'*-methylpyrazol-4-ylsulfonyl)-*N*-methylamino]pyrimidin-4-yl]-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-[5-(*N*-methyl-*N*-4-toluenesulfonylamino)pyrimidin-4-yl]-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine isopropyl ester,

N-[5-(*N*-methyl-*N*-3-pyridylsulfonylamino)pyrimidin-4-yl]-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine *tert*-butyl ester,

N-(5-(*N*-methyl-*N*-(1-butylpyrazol-4-yl)sulfonylamino)pyrimidin-4-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2,4-dimethoxypyrimidin-5-yl)pyrimidin-4-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2,6-difluorophenyl)pyrimidin-4-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2-hydroxymethylphenyl)pyrimidin-4-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-cyclohexylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-(1-methylpiperidin-4-yl)amino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-ethyl-*N*-isopropylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2,4-6-trimethylphenyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-isopropylpyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-butylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-ethyl-*N*-propylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N,N*-diethylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-ethylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-benzyloxypyrimidin-4-yl)-L-phenylalanine,

N-(5-benzyloxypyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(*N*-methyl-*N*-4-toluenesulfonylamino)pyrimidin-4-yl)-L-phenylalanine,

N-(5-(*N*-methyl-*N*-3-pyridinesulfonylamino)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-phenylpyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(3-(*N*-methyl-*N*-4-toluenesulfonylamino)pyrazin-2-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(*N*-methyl-*N*-3-pyridinesulfonylamino)pyrimidin-4-yl)-L-4-(4-methylpiperazin-1-ylcarbonyloxy)phenylalanine isopropyl ester,

N-(5-benzylpyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(*N*-methyl-*N*-3-pyridinesulfonylamino)pyrimidin-4-yl)-L-4-(4-methylpiperazin-1-ylcarbonyloxy)phenylalanine tert-butyl ester,

N-(5-(2-trifluoromethylphenyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2-*N,N*-dimethylcarbamylethyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(*N*-methyl-*N*-3-(1-methylpyrazole)sulfonylamino)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine isopropyl ester,

N-(6-phenylpyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(6-(2-trifluoromethylphenyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(6-(2-hydroxymethylphenyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-cyclohexylpyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-2-furanmethylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-4-chlorophenylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(3-thienyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2-thienyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-2-hydroxyethylamino)-5-(2-fluorophenyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(piperidin-1-yl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(1-propylbutyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclobutylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclobutylamino)-5-ethylpyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N,N*-bis-(2-hydroxyethyl)amino)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N,N*-bis-(2-hydroxyethyl)amino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-phenylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(isopropoxy)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(N-methyl-N-3-methylbutylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(2-tolyl)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-2-hydroxyethylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-2-methylpropylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-propylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N,N*-dimethylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)-5-(3-pyridyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2-phenyl-2,2-difluoroethyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2-phenyl-2,2-difluoroethyl)-6-chloropyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2-phenylethyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-propylpyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2-methoxyphenyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2-fluorophenyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-Methyl-*N*-isopropylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-isopropylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2-phenylethyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine isopropyl ester,

N-(3-(*N*-methyl-*N*-4-toluenesulfonylamino)pyrazin-2-yl)-L-phenylalanine isopropyl ester,

N-(5-(2-phenylethyl)pyrimidin-4-yl)-L-phenylalanine isopropyl ester,

N-(5-(*N*-methyl-*N*-3-pyridinesulfonylamino)pyrimidin-4-yl)-L-4-(4-methylpiperazin-1-ylcarbonyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine isopropyl ester,

N-(5-(3-nitrophenyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(3-pyridyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(2-phenylethyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-*N,N*-dimethylamino-5-(*N*-methyl-*N*-4-toluenesulfonylamino)pyrimidin-4-yl)-L-phenylalanine,

N-(5-(2-tolyl)pyrimidin-4-yl)-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)-5-(2-methoxyphenyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-isopropylamino)-5-(2-fluorophenyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-isopropylamino)-5-(2-fluorophenyl)pyrimidin-4-yl)-L-4-(2-methoxyphenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)-5-(2,6-difluorophenyl)pyrimidin-4-yl)-L-4-(2,6-difluorophenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)-5-(2-hydroxymethylphenyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(2-(*N,N*-bis-(2-hydroxyethyl)amino)-5-(2,4,6-trimethylphenyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)-5-(2-trifluoromethylphenyl)pyrimidin-4-yl)-L-4-(2-cyanophenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)-5-(3-thienyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)-5-(2-thienyl)pyrimidin-4-yl)-L-4-(4-trifluoromethylphenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)-5-(3-pyridyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)-5-(3-nitrophenyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)-5-(2,6-dichlorophenyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)-5-(4-pyridyl)pyrimidin-4-yl)-L-4-(3-hydroxymethylphenyl)phenylalanine,

N-(2-(*N*-ethyl-N-isopropylamino)-5-(2,6-dimethoxyphenyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)-5-(2,3-dichlorophenyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-ethylamino)-5-(2,4,6-trimethylphenyl)pyrimidin-4-yl)-L-4-(2-cyanophenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-isopropylamino)-5-(2,4,6-trimethylphenyl)pyrimidin-4-yl)-L-4-(3-pyridyl)phenylalanine,

N-(2-(*N*,*N*-bis-(2-hydroxyethyl)amino)-5-(2,4,6-trimethylphenyl)pyrimidin-4-yl)-L-4-(2-cyanophenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-(1-methylpiperidin-4-yl)amino)-5-(2-cyanophenyl)pyrimidin-4-yl)-L-4-(2,6-difluorophenyl)phenylalanine,

N-(2-(*N*-ethyl-N-isopropylamino)-5-(2,4,6-trimethylphenyl)pyrimidin-4-yl)-L-4-(o-tolyl)phenylalanine,

N-(2-(*N*-methyl-*N*-4-chlorophenylamino)-5-(2,4,6-trimethylphenyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(5-(*N*-methyl-N-2-(phenyl)ethylamino)pyrimidin-4-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(N-methyl-N-hexylamino)pyrimidin-4-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(N-methyl-N-isopropylamino)pyrimidin-4-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(N-methyl-N-*tert*-butylamino)pyrimidin-4-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(N-ethyl-N-isopropylamino)pyrimidin-4-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(N-methyl-N-2-(4-pyridyl)ethyl-pyrimidin-4-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-(5-(N-methyl-N-2-(phenyl)ethylamino)pyrimidin-4-yl)-L-4-(4-(2,6-dimethoxyphenyl)phenylalanine,

N-(5-(N-methyl-N-hexylamino)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(5-(N-methyl-N-isopropylamino)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(5-(N-methyl-N-*tert*-butylamino)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(5-(N-ethyl-N-isopropylamino)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(5-(N-methyl-N-2-(4-pyridyl)ethyl-pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(2-(*N*-methyl-*N*-cyclohexylamino)-5-ethylpyrimidin-4-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-(4-(N,N-di-*n*-hexylamino)-1,1-dioxo-1,2,5-thiadiazol-3-yl)-L-tyrosine,

N-(4-(N,N-di-*n*-hexylamino)-1,1-dioxo-1,2,5-thiadiazol-3-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine,

N-(4-(N,N-dimethylamino)-1-oxo-1,2,5-thiadiazol-3-yl)-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine *tert*-butyl ester,

N-[4-(2-(3-methylphenylaminocarbonylamino)eth-1-ylamino)-1,1-dioxo-1,2,5-thiadiazol-3-yl]-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine

N-(4-(N,N-di-*n*-hexylamino)-1,1-dioxo-1,2,5-thiadiazol-3-yl)-L-4-(4-methylpiperazin-1-ylcarbonyloxy)phenylalanine,

N-(5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(2-(N-cyclohexyl-N-methyl)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

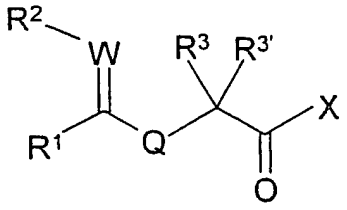
N-(5-(2-fluorophenyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(2-(N-methyl-N-propyl)-5-(2-tolyl)pyrimidin-4-yl)-L-4-(2,6-dimethoxyphenyl)phenylalanine,

N-(3-chloropyrazin-2-yl)-L-4-[1-(*tert*-butoxycarbonyl)piperidin-4-ylcarbonylamino]phenylalanine ethyl ester,

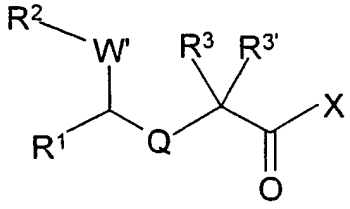
and pharmaceutically acceptable salts thereof.

51. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of formula Ia and/or Ib:



Ia

and



Ib

wherein, in formula Ia, R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form an aryl, cycloalkenyl, heteroaryl or heterocyclic group having at least five atoms in the aryl, cycloalkenyl, heteroaryl or heterocyclic group and optionally containing or additionally containing in the case of heteroaryl and

heterocyclic groups 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur, and wherein the heteroaryl or heterocyclic group is mono-cyclic;

in formula Ib, R^1 and R^2, together with the carbon atom and W' to which they are bound respectively, are joined to form a cycloalkyl, cycloalkenyl or heterocyclic group having at least five atoms in the cycloalkyl, cycloalkenyl or heterocyclic group and optionally containing or additionally containing in the case of the heterocyclic group 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur, and wherein the heterocyclic group is mono-cyclic;

and further wherein said aryl, cycloalkyl, cycloalkenyl, heteroaryl or heterocyclic group of formula Ia or Ib is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, $-OS(O)_2$-alkyl, $-OS(O)_2$-substituted alkyl, $-OS(O)_2$-aryl, $-OS(O)_2$-substituted aryl, $-OS(O)_2$-heteroaryl, $-OS(O)_2$-substituted heteroaryl, $-OS(O)_2$-heterocyclic, $-OS(O)_2$-substituted heterocyclic, $-OSO_2$-NRR where each R is independently hydrogen or alkyl, $-NRS(O)_2$-alkyl, -

$NRS(O)_2$-substituted alkyl, $-NRS(O)_2$-aryl, $-NRS(O)_2$-substituted aryl, $-NRS(O)_2$-heteroaryl, $-NRS(O)_2$-substituted heteroaryl, $-NRS(O)_2$-heterocyclic, $-NRS(O)_2$-substituted heterocyclic, $-NRS(O)_2$-NR-alkyl, $-NRS(O)_2$-NR-substituted alkyl, $-NRS(O)_2$-NR-aryl, $-NRS(O)_2$-NR-substituted aryl, $-NRS(O)_2$-NR-heteroaryl, $-NRS(O)_2$-NR-substituted heteroaryl, $-NRS(O)_2$-NR-heterocyclic, $-NRS(O)_2$-NR-substituted heterocyclic where R is hydrogen or alkyl, $-N[S(O)_2-R']_2$ and $-N[S(O)_2-NR']_2$ where each R′ is independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^3 is $-(CH_2)_x$-Ar-R^9, where Ar is aryl, substituted aryl, heteroaryl and substituted heteroaryl; R^9 is selected from the group consisting of acyl, acylamino, acyloxy, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, oxycarbonylamino, oxythiocarbonylamino, thioamidino, thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl, oxysulfonylamino and oxysulfonyl, and *x* is an integer from 0 to 4;

$R^{3'}$ is selected from the group consisting of hydrogen, isopropyl, $-CH_2Z$ where Z is selected from the group consisting of hydrogen, hydroxyl, acylamino, alkyl, alkoxy, aryloxy, aryl, aryloxyaryl, carboxyl, carboxylalkyl, carboxyl-substituted alkyl, carboxyl-cycloalkyl, carboxyl-substituted cycloalkyl, carboxylaryl, carboxyl-substituted aryl, carboxylheteroaryl, carboxyl-substituted heteroaryl, carboxylheterocyclic, carboxyl-substituted heterocyclic, cycloalkyl, substituted alkyl, substituted alkoxy, substituted aryl, substituted aryloxy, substituted aryloxyaryl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

Q is selected from the group consisting of -O-, -S-, -S(O)-, $-S(O)_2$, and $-NR^4$-;

R^4 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic or, optionally, R^4 and R^1 or R^4 and R^2, together with the atoms to which they are bound, are joined to form a heteroaryl, a substituted heteroaryl, a heterocyclic or a substituted heterocyclic group;

W is selected from the group consisting of nitrogen and carbon; and

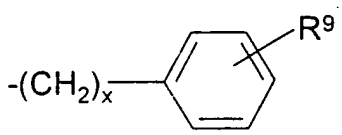
W' is selected from the group consisting of nitrogen, carbon, oxygen, sulfur, S(O), and $S(O)_2$;

X is selected from the group consisting of hydroxyl, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, cycloalkoxy, substituted cycloalkoxy, cycloalkenoxy, substituted cycloalkenoxy, aryloxy, substituted aryloxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy and -NR"R" where each R" is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

and enantiomers, diasteromers and pharmaceutically acceptable salts thereof;

and further wherein the compound of formula Ia and/or Ib has a binding affinity to VLA-4 as expressed by an IC_{50} of about 15 μM or less.

52. The pharmaceutical composition of Claim 51, wherein R^3 is a group of the formula:



wherein R^9 and x are as defined in Claim 47; and $R^{3'}$ is hydrogen.

53. The pharmaceutical composition of Claim 52, wherein R^9 is in the *para* position of the phenyl ring; and x is an integer from 1 to 4.

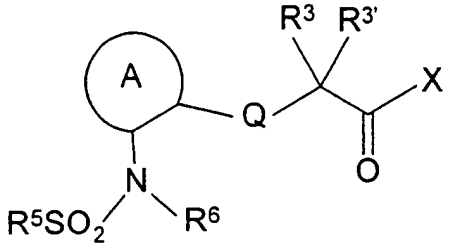
54. The pharmaceutical composition of Claim 53, wherein R^9 is selected from the group consisting of -O-Z-$NR^{11}R^{11'}$ and -O-Z-R^{12} wherein R^{11} and $R^{11'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R^{11} and $R^{11'}$ are joined to form a heterocycle or a substituted heterocycle, R^{12} is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of -C(O)- and -SO_2-.

55. The pharmaceutical composition of Claim 54, wherein Z is -C(O)-.

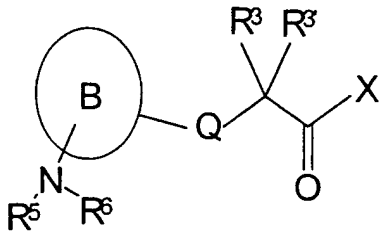
56. The pharmaceutical composition of Claim 55, wherein R^9 is -OC(O)$NR^{11}R^{11'}$.

57. The pharmaceutical composition of Claim 51, wherein Q is -NR^4-.

58. The pharmaceutical composition of Claim 51, wherein the compound has formula IIa or IIb:



IIa



IIb

wherein

ring A and ring B form a heteroaryl or substituted heteroaryl group having two nitrogen atoms in the heteroaryl ring;

R^5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and $-SO_2R^{10}$ where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

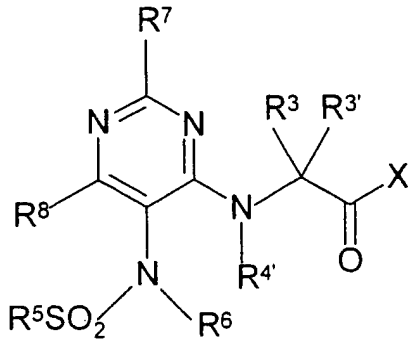
or optionally, one of, R^4 and ring A, R^4 and R^5, R^4 and R^6, or R^5 and R^6, together with the atoms to which they are bound, can be joined to form a heterocyclic or substituted heterocyclic ring;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof; and provided that ring B does not form a 6-amino or substituted amino pyrimidin-4-yl group.

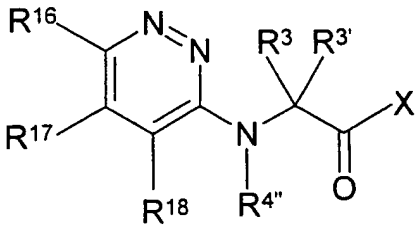
59. The pharmaceutical composition of Claim 58, wherein ring A forms a pyridazine, pyrimidine or pyrazine ring, wherein the pyridazine, pyrimidine or pyrazine ring is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen, and

ring B forms a pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or a 1,1-dioxo-1,2,5-thiadiazole ring, wherein the pyridazine, pyrimidine or pyrazine ring is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

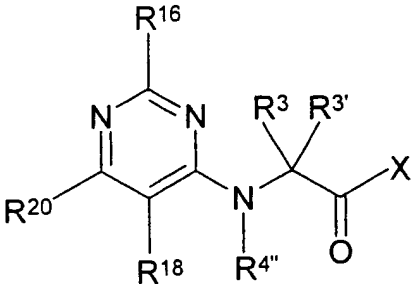
60. The pharmaceutical composition of Claim 51, wherein the compound has formula IIIa, IIIc, IIId, IIIe or IIIf:



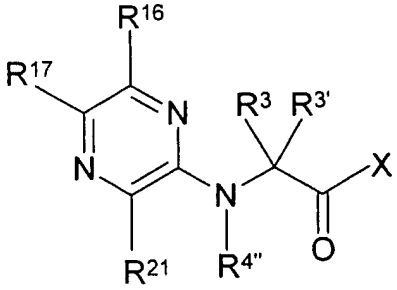
IIIa



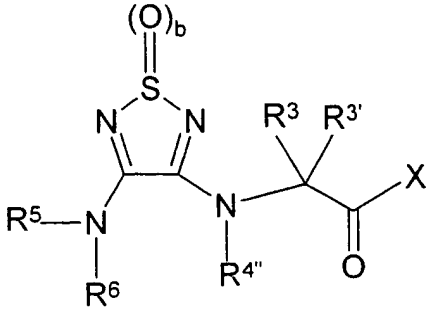
IIIc



IIId



IIIe



IIIf

wherein

$R^{4'}$ is selected from the group consisting of hydrogen and alkyl or, optionally, one of, $R^{4'}$ and R^5, $R^{4'}$ and R^6, R^5 and R^6, R^5 and R^8, or R^6 and R^8, together with the atoms to which they are bound, are joined to form a heterocyclic, a substituted heterocyclic, a heteroaryl or substituted heteroaryl group optionally containing from 1 to 3 additional hetero ring atoms selected from the group consisting of oxygen, nitrogen and sulfur;

$R^{4''}$ is selected from the group consisting of hydrogen and alkyl;

R^5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and $-SO_2R^{10}$ where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

R^7 and R^8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{16} and R^{17} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R^{18} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{20} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

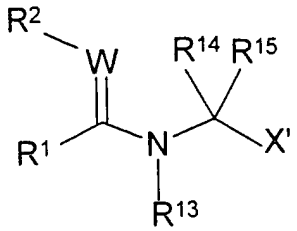
R^{21} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

61. The pharmaceutical composition of Claim 60, wherein the compound is selected from formula IIId, IIIe or IIIf.

62. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of formula IVa:



IVa

wherein R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a heteroaryl group having two nitrogen atoms;

and further wherein said heteroaryl group is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, $-OS(O)_2$-alkyl, $-OS(O)_2$-substituted alkyl, $-OS(O)_2$-aryl, $-OS(O)_2$-substituted aryl, $-OS(O)_2$-heteroaryl, $-OS(O)_2$-substituted heteroaryl, $-OS(O)_2$-heterocyclic, $-OS(Q)_2$-substituted heterocyclic, $-OSO_2$-NRR where each R is independently hydrogen or alkyl, $-NRS(O)_2$-alkyl, $-NRS(O)_2$-substituted alkyl, $-NRS(O)_2$-aryl, $-NRS(O)_2$-substituted aryl, $-NRS(O)_2$-heteroaryl, $-NRS(O)_2$-substituted heteroaryl, $-NRS(O)_2$-heterocyclic, $-NRS(O)_2$-substituted heterocyclic, $-NRS(O)_2$-NR-alkyl, $-NRS(O)_2$-NR-substituted alkyl, $-NRS(O)_2$-NR-aryl, $-NRS(O)_2$-NR-substituted aryl, $-NRS(O)_2$-NR-heteroaryl, $-NRS(O)_2$-NR-substituted heteroaryl, $-NRS(O)_2$-NR-heterocyclic, $-NRS(O)_2$-NR-substituted heterocyclic where R is hydrogen or alkyl, $-N[S(O)_2-R']_2$ and $-N[S(O)_2-NR']_2$ where each R′ is independently selected from the group consisting of alkyl, substituted alkyl,

aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{13} is selected from the group consisting of hydrogen, C_{1-10} alkyl, Cy, and Cy-C_{1-10} alkyl, wherein alkyl is optionally substituted with one to four substituents independently selected from R^a; and Cy is optionally substituted with one to four substituents independently selected from R^b;

R^{14} is selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, Cy, Cy-C_{1-10} alkyl, Cy-C_{2-10} alkenyl and Cy-C_{2-10} alkynyl, wherein alkyl, alkenyl, and alkynyl are optionally substituted with one to four substituents selected from phenyl and R^X, and Cy is optionally substituted with one to four substituents independently selected from R^y;

or R^{13}, R^{14} and the atoms to which they are attached together form a mono- or bicyclic ring containing 0-2 additional heteratoms selected from N, O and S;

R^{15} is selected from the group consisting of C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl, aryl-C_{1-10} alkyl, heteroaryl, heteroaryl-C_{1-10} alkyl, wherein alkyl, alkenyl and alkynyl are optionally substituted with one to four substituents selected from R^x, and aryl and heteroaryl are optionally substituted with one to four substituents independently selected from R^y;

or R^{14}, R^{15} and the carbon to which they are attached form a 3-7 membered mono- or bicyclic ring containing 0-2 heteroatoms selected from N, O and S;

R^a is selected from the group consisting of Cy and a group selected from R^x, wherein Cy is optionally substituted with one to four substituents independently selected from R^c;

R^b is selected from the group consisting of R^a, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl C_{1-10}alkyl, heteroaryl C_{1-10} alkyl, wherein alkyl, alkenyl, alkynyl, aryl, heteroaryl are optionally substituted with a group independently selected from R^c;

R^c is selected from the group consisting of halogen, NO_2, $C(O)OR^f$,

C_{1-4} alkyl, C_{1-4} alkoxy, aryl, aryl C_{1-4} alkyl, aryloxy, heteroaryl, NR^fR^g, $R^fC(O)R^g$, $NR^fC(O)NR^fR^g$, and CN;

R^d and R^e are independently selected from hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, Cy and Cy C_{1-10}alkyl, wherein alkyl, alkenyl, alkynyl and Cy are optionally substituted with one to four substituents independently selected from R^c;

or R^d and R^e together with the atoms to which they are attached form a heterocyclic ring of 5 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and nitrogen;

R^f and R^g are independently selected from hydrogen, C_{1-10} alkyl, Cy and Cy-C_{1-10} alkyl wherein Cy is optionally substituted with C_{1-10} alkyl; or R^f and R^g together with the carbon to which they are attached form a ring of 5 to 7 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and nitrogen;

R^h is selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, cyano, aryl, aryl C_{1-10} alkyl, heteroaryl, heteroaryl C_{1-10} alkyl, and $-SO_2R^i$; wherein alkyl, alkenyl, and alkynl are optionally substituted with one to four substitutents independently selected from R^a; and aryl and heteroaryl are each optionally substituted with one to four substituents independently selected from R^b;

R^i is selected from the group consisting of C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, and aryl; wherein alkyl, alkenyl, alkynyl and aryl are each optionally substituted with one to four substituents independently selected from R^c; .

R^x is selected from the group consisting of $-OR^d$, $-NO_2$, halogen, $-S(O)_mR^d$, $-SR^d$, $-S(O)_2OR^d$, $-S(O)_mNR^dR^e$, $-NR^dR^e$, $-O(CR^fR^g)_nNR^dR^e$, $-C(O)R^d$, $-CO_2R^d$, $-CO_2(CR^fR^g)_nCONR^dR^e$, $-OC(O)R^d$, -CN, $-C(O)NR^dR^e$, $-NR^dC(O)R^e$, $-OC(O)NR^dR^e$, $-NR^dC(O)OR^e$, $-NR^dC(O)NR^dR^e$, $-CR^d(N\text{-}OR^e)$, CF_3, oxo, $NR^dC(O)NR^dSO_2R^i$, $NR^dS(O)_mR^e$, $-OS(O)_2OR^d$, and $-OP(O)(OR^d)_2$;

R^y is selected from the group consisting of R^x, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl C_{1-10}alkyl, heteroaryl C_{1-10} alkyl, cycloalkyl, heterocyclyl; wherein alkyl, alkenyl, alkynyl and aryl are each optionally substituted with one to four substitutents independently selected from R^x;

Cy is cycloalkyl, heterocyclyl, aryl, or heteroaryl;

m is an integer from 1 to 2;

n is an integer from 1 to 10;

W is selected from the group consisting of carbon and nitrogen;

W' is selected from the group consisting of carbon, nitrogen, oxygen, sulfur, S(O) and $S(O)_2$;

X' is selected from the group consisting of $-C(O)OR^d$, $-P(O)(OR^d)(OR^e)$, $-P(O)(R^d)(OR^e)$, $-S(O)_mOR^d$, $-C(O)NR^dR^h$, and -5-tetrazolyl;

and enatiomers, diastereomers and pharmaceutically acceptable salts thereof;

and further wherein the compound of formula IV has a binding affinity to VLA-4 as expressed by an IC_{50} of about 15μM or less;

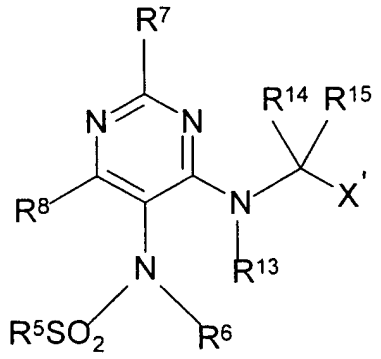
and provided that when R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a 2-arylpyrimidin-4-yl group and R^{14} is hydrogen, then R^{15} is not alkyl of from 1 to 6 carbon atoms optionally substituted with hydroxyl; and when R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a 5-arylpyrazin-2-yl group and R^{14} is hydrogen, then R^{15} is not 4-hydroxybenzyl.

63. The pharmaceutical composition of Claim 62, wherein R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or 1,1-dioxo-1,2,5-thiadiazole ring; wherein the pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or a 1,1-dioxo-1,2,5-

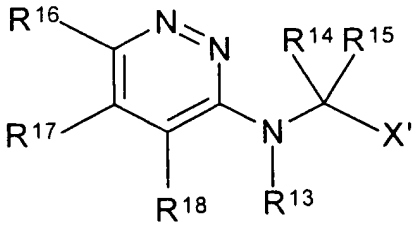
thiadiazole ring is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

64. The pharmaceutical composition of Claim 62, wherein X' is $-C(O)OR^d$.

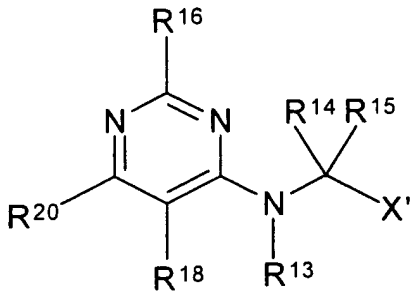
65. The pharmaceutical composition of Claim 62, wherein the compound has formula Va, Vc, Vd, Ve or Vf:



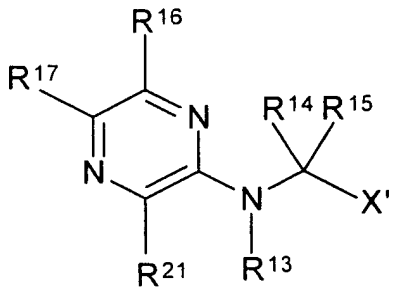
Va



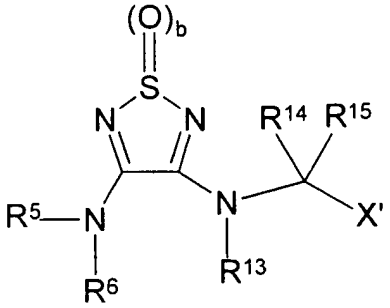
Vc



Vd



Ve



Vf

wherein

R^5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted

cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and $-SO_2R^{10}$ where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl; and

R^7 and R^8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{16} and R^{17} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R^{18} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{20} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

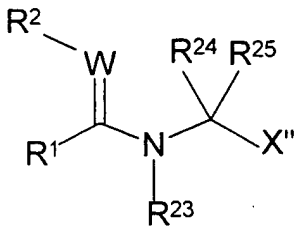
R^{21} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2;

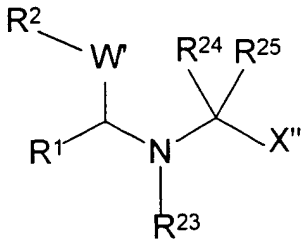
and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

66. The pharmaceutical composition of Claim 65, wherein the compound is selected from formula Vd, Ve or Vf.

67. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of formula VIa and/or VIb:



and



VIa VIb

wherein, in formula VIa, R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form an aryl, cycloalkenyl, heteroaryl or heterocyclic group having at least five atoms in the aryl, cycloalkenyl, heteroaryl or heterocyclic group and optionally containing or additionally containing in the case of heteroaryl and heterocyclic groups 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur, and wherein the heteroaryl or heterocyclic group is mono-cyclic;

in formula VIb, R^1 and R^2, together with the carbon atom and W' to which they are bound respectively, are joined to form a cycloalkyl, cycloalkenyl or heterocyclic group having at least five atoms in the cycloalkyl, cycloalkenyl or heterocyclic group and optionally containing or additionally containing in the case of the heterocyclic group 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur, and wherein the heterocyclic group is mono-cyclic;

and further wherein said aryl, cycloalkyl, cycloalkenyl, heteroaryl or heterocyclic group of formula VIa or VIb is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, $-OS(O)_2$-alkyl, $-OS(O)_2$-substituted alkyl, $-OS(O)_2$-aryl, $-OS(O)_2$-substituted aryl, $-OS(O)_2$-heteroaryl, $-OS(O)_2$-substituted heteroaryl, $-OS(O)_2$-heterocyclic, $-OS(O)_2$-substituted heterocyclic, $-OSO_2$-NRR where each R is independently hydrogen or alkyl, $-NRS(O)_2$-alkyl, $-NRS(O)_2$-substituted alkyl, $-NRS(O)_2$-aryl, $-NRS(O)_2$-substituted aryl, $-NRS(O)_2$-heteroaryl, $-NRS(O)_2$-substituted heteroaryl, $-NRS(O)_2$-heterocyclic, $-NRS(O)_2$-substituted heterocyclic, $-NRS(O)_2$-NR-alkyl, $-NRS(O)_2$-NR-substituted alkyl, $-NRS(O)_2$-NR-aryl, $-NRS(O)_2$-NR-substituted aryl, $-NRS(O)_2$-NR-heteroaryl, $-NRS(O)_2$-NR-substituted heteroaryl, $-NRS(O)_2$-NR-heterocyclic, $-NRS(O)_2$-NR-substituted heterocyclic where R is hydrogen or alkyl, $-N[S(O)_2-R']_2$ and $-N[S(O)_2-NR']_2$ where each R′ is independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{23} is selected from the group consisting of hydrogen, C_{1-10} alkyl optionally substituted with one to four substituents independently selected from $R^{a'}$ and Cy optionally substituted with one to four substituents independently selected from $R^{b'}$;

R^{24} is selected from the group consisting of Ar^1-Ar^2-C_{1-10} alkyl, Ar^1-Ar^2-C_{2-10} alkenyl, Ar^1-Ar^2-C_{2-10} alkynyl, wherein Ar^1 and Ar^2 are independently aryl or heteroaryl each of which is optionally substituted with one to four substituents independently selected from $R^{b'}$; alkyl, alkenyl and alkynyl are optionally substituted with one to four substituents independently selected from $R^{a'}$;

R^{25} is selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl, aryl C_{1-10}alkyl, heteroaryl, and heteroaryl C_{1-10} alkyl, wherein alkyl, alkenyl and alkynyl are optionally substituted with one to four substituents selected from $R^{a'}$, and aryl and heteroaryl are optionally substituted with one to four substituents independently selected from $R^{b'}$;

$R^{a'}$ is selected from the group consisting of Cy, $-OR^{d'}$, $-NO_2$, halogen $-S(O)_mR^{d'}$, $-SR^{d'}$, $-S(O)_2OR^{d'}$, $-S(O)_mNR^{d'}R^{e'}$, $-NR^{d'}R^{e'}$, $-O(CR^{f'}R^{g'})_nNR^{d'}R^{e'}$, $-C(O)R^{d'}$, $-CO_2R^{d'}$, $-CO_2(CR^{f'}R^{g'})_nCONR^{d'}R^{e'}$, $-OC(O)R^{d'}$, $-CN$, $-C(O)NR^{d'}R^{e'}$, $-NR^{d'}C(O)R^{e'}$, $-OC(O)NR^{d'}R^{e'}$, $-NR^{d'}C(O)OR^{e'}$, $-Nr^{d'}C(O)NR^{d'}R^{e'}$, $-CR^{d'}(N\text{-}OR^{e'})$, CF_3, and $-OCF_3$;

wherein Cy is optionally substituted with one to four substituents independently selected from $R^{c'}$;

$R^{b'}$ is selected from the group consisting of $R^{a'}$, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl C_{1-10} alkyl, heteroaryl C_{1-10}alkyl,

wherein alkyl, alkenyl, aryl, heteroaryl are optionally substituted with a group independently selected from $R^{c'}$;

$R^{c'}$ is selected from the group consisting of halogen, amino, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, aryl, aryl C_{1-4}alkyl, hydroxy, CF_3, and aryloxy;

$R^{d'}$ and $R^{e'}$ are independently selected from hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, Cy and Cy C_{1-10}alkyl, wherein alkyl, alkenyl, alkynyl and Cy are optionally substituted with one to four substituents independently selected from $R^{c'}$; or $R^{d'}$ and $R^{e'}$ together with the atoms to which they are attached form a heterocyclic ring of 5 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and nitrogen;

$R^{f'}$ and $R^{g'}$ are independently selected from hydrogen, C_{1-10} alkyl, Cy and Cy-C_{1-10} alkyl; or $R^{f'}$ and $R^{g'}$ together with the carbon to which they are attached form a ring of 5 to 7 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and nitrogen;

$R^{h'}$ is selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, cyano, aryl, aryl C_{1-10} alkyl, heteroaryl, heteroaryl C_{1-10} alkyl, or $-SO_2R^{i'}$;

wherein alkyl, alkenyl, and alkynyl are optionally substituted with one to four substitutents independently selected from $R^{a'}$; and aryl and heteroaryl are each optionally substituted with one to four substituents independently selected from $R^{b'}$;

$R^{i'}$ is selected from the group consisting of C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, and aryl;

wherein alkyl, alkenyl, alkynyl and aryl are each optionally substituted with one to four substituents independently selected from $R^{c'}$;

Cy is cycloalkyl, heterocyclyl, aryl, or heteroaryl;

X" is selected from the group consisting of $-C(O)OR^{d'}$, $-P(O)(OR^{d'})(OR^{e'})$, $-P(O)(R^{d'})(OR^{e'})$, $-S(O)_mOR^{d'}$, $-C(O)NR^{d'}R^{h'}$, and -5-tetrazolyl;

m is an integer from 1 to 2;

n is an integer from 1 to 10;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof;

and further wherein the compounds of formula VIa and/or VIb have a binding affinity to VLA-4 as expressed by an IC_{50} of about 15 μM or less.

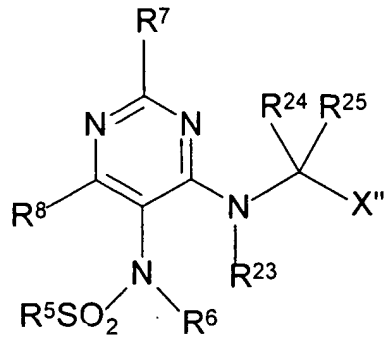
68. The pharmaceutical composition of Claim 67, wherein R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a heteroaryl or substituted heteroaryl group having two nitrogen atoms in the heteroaryl ring.

69. The pharmaceutical composition of Claim 68, wherein R^1 and R^2, together with the carbon atom and W to which they are bound respectively, are joined to form a pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or 1,1-dioxo-1,2,5-thiadiazole ring; wherein the pyridazine, pyrimidine, pyrazine, 1-oxo-1,2,5-thiadiazole or 1,1-dioxo-1,2,5-thiadiazole ring is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

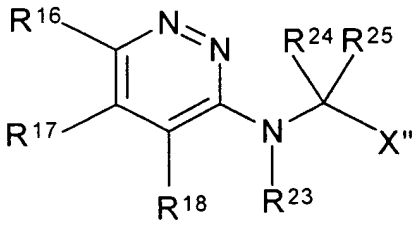
70. The pharmaceutical composition of Claim 67, wherein X" is $-C(O)OR^{d'}$.

71. The pharmaceutical composition of Claim 67, wherein R^{24} is $-CH_2-Ar^2-Ar^1$ and R^{25} is hydrogen.

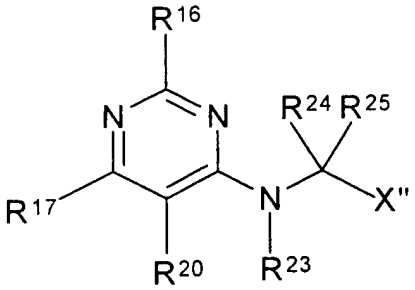
72. The pharmaceutical composition of Claim 67, wherein the compound has formula VIIa, VIIc, VIId, VIIe or VIIf:



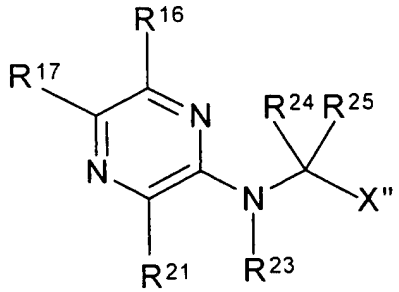
VIIa



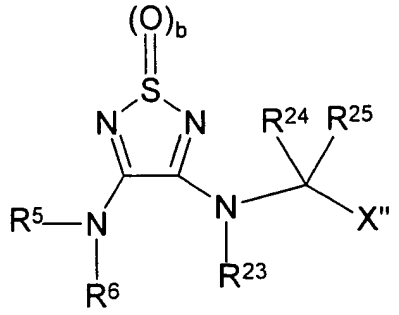
VIIc



VIId



VIIe



VIIf

wherein

R^5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and $-SO_2R^{10}$ where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl; and

R^7 and R^8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{16} and R^{17} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R^{18} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted

cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{20} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{21} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

73. The pharmaceutical composition of Claim 72, wherein the compound is selected from formula VIId, VIIe or VIIf.

74. A method for binding VLA-4 in a biological sample which method comprises contacting the biological sample with a compound of Claims 27, 38, 43 or 50 under conditions wherein said compound binds to VLA-4.